REMARKS

Claims 19, 20, 26, 30, 32-35, 37, 38, 40, 41, 43, 44, 46, and 47 are pending in the present application.

Applicants acknowledge that USSN 09/076,447, which was listed in a previously filed Information Disclosure Statement, is stated by the Examiner to not be in the IFW system. Accordingly, in response to the Examiner's request, Applicants will endeavor to submit a copy thereof shortly.

The Specification has been amended herein to more accurately refer to Figure 6 than Figure 5. Applicants' undersigned representative thanks the Examiner for pointing out this typographical error.

I. The Claimed Invention Is Not Obvious

Claims 19, 20, 26, 30, 32-35, 37, 38, 40, 41, 43, 44, 46, and 47 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the combination of the following references: 1) Murray et al., J. Computer-Aided Mol. Des., 1997, 11, 193-207 (hereinafter, the "Murray reference"), 2) U.S. Patent No. 6,337,183 (hereinafter, the "Arenas reference"), 3) Sezerman et al., Protein Sci., 1993, 2, 1827-1843 (hereinafter, the "Sezerman reference"), 4) Greig et al., J. Am. Chem. Soc., 1995, 117, 10765-10766 (hereinafter, the "Greig reference"), and 5) Hentze et al., Science, 1987, 238, 1570-1573 (hereinafter, the "Hentze reference"). The Action asserts:

> It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the screening method of Murray et al. by use of the RNA targets of Arenas et al. because Arenas et al. shows bioassays that screen for compounds that bind to RNA targets. It would have been further obvious to use mass spectroscopy to analyze binding strength because Sezerman shows that peptides may be analyzed in silico for binding, and Greig et al. shows that mass spectroscopy may be used to determine the binding affinity of a complex of a peptide and an oligonucleotide, and experimental determination of binding strength is an important parameter for determination of biological activity. It would have been further obvious to use the IRE target sequence of Hentze et al. because Hentze et al. shows that the human IRE RNA target sequence has a role in cell iron metabolism, and further can be used to confer regulation of translation on a mRNA of choice. Development of compounds that bind to the human IRE would allow for development of

> compounds that inhibit or enhance expression of wild type or recombinant genes in human cells as suggested by Arenas to allow for insights into the function of naturally occurring mRNA or to regulate gene expression of recombinant genes comprising the IRE.

(See, Office Action at page 7). Applicants traverse the rejection and respectfully request reconsideration because there is no motivation to combine the cited references and, even if combined, the claimed invention would not be produced.

It cannot fairly be said that the combination of cited references, which does not so much as mention some features recited in the claimed methods, render such methods obvious. Thus, rejection under §103 is improper since a case of *prima facie* obviousness cannot be made. *In re Payne*, 203 USPQ 245, 255 (CCPA 1979) (references relied upon to support rejection under §103 must place the claimed invention in the possession of the public). For example, claim 26 recites, in relevant part: "identifying *in silico* at least one molecular interaction site less than 30 nucleotides in length on said human target RNA **by comparing the nucleotide sequence of said human target RNA with the nucleotide sequence of a RNA from a different taxonomic species, identifying at least one conserved region, and determining the secondary structure of said conserved region**" (emphasis added). Applicants' undersigned representative has not been able to locate any portion of the cited references which teach these features. Further, the Office does not identify any portion of the cited references that teach these features either. Thus, even if the cited references are combined in the manner suggested by the Office, the invention recited in claim 26, as well as claims dependent thereon (i.e., claims 30, 40, and 41), is not produced.

The Office also fails to make out a *prima facie* case of obviousness in regard to the remaining independent claims. When making a *prima facie* case of obviousness, it remains necessary to identify some reason that would have led a person skilled in the art to modify the teachings of a reference in a particular manner. *Takeda Chemical Industries, Ltd. v Alphapharm Pty. Ltd.*, 492 F.3d 1350, 83 USPQ.2d 1169 (Fed. Cir. 2007). No such reasoning has been provided. Indeed, there are many possibilities from which to choose for "testing said highly ranked members to determine their ability to interact with said molecular interaction site." There is, however, nothing in the prior art to narrow these possibilities to that which is recited in

Applicants' claims (i.e., "contacting the human target RNA with at least one of said highly ranked members to provide a complex between the human target RNA and the member or members; ionizing said complex; fragmenting the ionized complex; and determining whether highly ranked members bind to the molecular interaction site of said human target RNA"). It is only upon examination of Applicants' specification that such claimed methods can be rendered obvious. Applicants respectfully point out that "[i]t is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious." *In re Fritch*, 23 USPQ.2d 1780, 1784 (Fed. Cir. 1992).

In addition, if a proposal for modifying the prior art in an effort to attain the claimed invention causes the art to become inoperable or destroys its intended function, then the requisite motivation to make the modification would not have existed. *See In re Fritch*, 972 F.2d at 1265 n.12 ("A proposed modification [is] inappropriate for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose."); *In re Ratti*, 270 F.2d 810, 813 (CCPA 1959) (holding the suggested combination of references improper under §103 because it "would require a substantial reconstruction and redesign of the elements shown in [a prior art reference] as well as a change in the basic principles under which [that reference's] construction was designed to operate"). In this regard, the Murray reference reports an *in silico* method of identifying virtual compounds that can bind to a particular site within a molecule. Indeed, the Murray reference reports identification of thrombin inhibitors by a completely *in silico* method, in contrast to actually carrying out physical binding assays. Thus, a major goal of the Murray reference is to provide an *in silico* method, rather than actual physical methods, of predicting binding of a potential therapeutic compound to a particular receptor. Any modification of the Murray reference that would add another layer of a completely different, let alone physical, technology such as mass spectrometry, would be counter to the *in silico* methodology of the Murray reference. Therefore, the requisite motivation to further modify the methodology of the Murray reference does not exist. In this regard, each of claims 19 (and dependent claims 20, 37, and 38), 32 (and dependent claims 33, 43, and 44), and 34 (and dependent claims 35, 46, and 47) recite "testing said highly ranked members to determine their ability to interact with said molecular interaction site by: contacting the human target RNA with

at least one of said highly ranked members to provide a complex between the human target RNA and the member or members; ionizing said complex; fragmenting the ionized complex; and determining whether highly ranked members bind to the molecular interaction site of said human target RNA" or something similar thereto, and therefore are not obvious over the combination of cited references. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

II. The Claimed Invention Is Supported by Ample Written Description

Claims 19, 20, 26, 30, 32-35, 37, 38, 40, 41, 43, 44, 46, and 47 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Office asserts that the specification "does not describe human target RNA sequences with an interaction site that is **less** than 30 nucleotides in length" (emphasis in Action, see page 4). Applicants traverse the rejection and respectfully request reconsideration because the specification provides ample written description supporting the claims.

As a preliminary matter, claim 19, for example, recites, in relevant part:

> generating *in silico* a virtual library of compounds and an *in silico* three dimensional representation of a molecular interaction site within said human target RNA, **wherein the molecular interaction site is less than 30 nucleotides**;

(emphasis added). Thus, claim 19 recites that it is the molecular interaction site that is less than 30 nucleotides, and not the "human target RNA sequences with an interaction site that is **less** than 30 nucleotides," as suggested by the Office.

As stated in the previously filed response, Applicants' specification teaches:

> Applicants' invention is directed to methods of identifying secondary structures in eukaryotic and prokaryotic RNA molecules termed "molecular interaction sites." **Molecular interaction sites are** small, usually **less than 30 nucleotides**, independently folded, functional subdomains contained within a larger RNA molecule.

(see, page 15, line 30 to page 16, line 2 of the specification). Thus, this portion of the specification alone provides ample written description showing that Applicants were in possession of the claimed invention.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, as allegedly failing to provide sufficient written description be withdrawn.

III. Conclusion

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Office is invited to contact Applicants' undersigned representative at (610) 640-7859 if there are any questions regarding Applicants' claimed invention.

The Commissioner is hereby authorized to debit any underpayment of fee due or credit any overpayment to Deposit Account No. 50-0436.

Respectfully submitted,

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